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ENTRY

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TOTAL

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SESSION

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=> s HAUSP and MDM2

51 HAUSP

2970 MDM2

L1 21 HAUSP AND MDM2

=> s 11 not py>2004

2147267 PY>2004

L2 6 L1 NOT PY>2004

=> d ibib 1-6

L2 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:63694 CAPLUS

DOCUMENT NUMBER: 143:224203

TITLE: Dynamics in the p53-Mdm2 ubiquitination

pathway

AUTHOR(S): Brooks, Christopher L.; Gu, Wei

CORPORATE SOURCE: Institute for Cancer Genetics and Department of

Pathology; College of Physicions and Surgeons,

Columbia University, New York, NY, USA

SOURCE: Cell Cycle (2004), 3(7), 895-899

CODEN: CCEYAS; ISSN: 1538-4101

PUBLISHER: Landes Bioscience

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:60430 CAPLUS

DOCUMENT NUMBER: 142:215611

TITLE: HAUSP is required for p53 destabilization

AUTHOR(S): Cummins, Jordan M.; Vogelstein, Bert

CORPORATE SOURCE: The Howard Hughes Medical Institute, The Sidney Kimmel

Comprehensive Cancer Center, Program in Cellular and Molecular Medicine, The Johns Hopkins University

Medical Institutions, Baltimore, MD, USA

medical institutions, Baltimore, MD,

SOURCE: Cell Cycle (2004), 3(6), 689-692 CODEN: CCEYAS; ISSN: 1538-4101 PUBLISHER: Landes Bioscience

DOCUMENT TYPE: Journal LANGUAGE: English

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:900604 CAPLUS

DOCUMENT NUMBER: 142:4278

TITLE: HAUSP/USP7 as an Epstein-Barr virus target

AUTHOR(S): Holowaty, M. N.; Frappier, L.

CORPORATE SOURCE: Department of Medical Genetics and Microbiology,

University of Toronto, Toronto, Can.

SOURCE: Biochemical Society Transactions (2004), 32(5),

731-732

CODEN: BCSTB5; ISSN: 0300-5127

PUBLISHER: Portland Press Ltd.

DOCUMENT TYPE: Journal LANGUAGE: English

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:398363 CAPLUS

DOCUMENT NUMBER: 141:121361

AUTHOR(S):

SOURCE:

TITLE: P53 apoptotic pathway molecules are frequently and

simultaneously altered in nonsmall cell lung carcinoma Mori, Shoichi; Ito, Genshi; Usami, Noriyasu; Yoshioka, Hiromu; Ueda, Yuichi; Kodama, Yoshinori; Takahashi,

Masahide; Fong, Kwun M.; Shimokata, Kaoru; Sekido,

Yoshitaka

CORPORATE SOURCE: Department of Clinical Preventive Medicine, Department

of Thoracic Surgery, Nagoya University School of

Medicine, Nagoya, Japan

SOURCE: Cancer (New York, NY, United States) (2004), 100(8),

1673-1682

CODEN: CANCAR; ISSN: 0008-543X

PUBLISHER: John Wiley & Sons, Inc.

DOCUMENT TYPE: Journal LANGUAGE: English

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:312009 CAPLUS

DOCUMENT NUMBER: 140:300911

TITLE: A dynamic role of HAUSP in the p53-

Mdm2 pathway

AUTHOR(S): Li, Muyang; Brooks, Christopher L.; Kon, Ning; Gu, Wei

CORPORATE SOURCE: Institute for Cancer Genetics and Department of

Pathology College of Physicians and Surgeons, Columbia

University, New York, NY, 10032, USA Molecular Cell (2004), 13(6), 879-886

CODEN: MOCEFL; ISSN: 1097-2765

PUBLISHER: Cell Press
DOCUMENT TYPE: Journal
LANGUAGE: English

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:312567 CAPLUS

DOCUMENT NUMBER: 137:44608

TITLE: Deubiquitination of p53 by HAUSP is an

important pathway for p53 stabilization

AUTHOR(S): Li, Muyang; Chen, Delin; Shiloh, Ariel; Luo, Jianyuan;

Nikolaev, Anatoly Y.; Qin, Jun; Gu, Wei

CORPORATE SOURCE: Institute for Cancer Genetics, and Department of

Pathology, College of Physicians b Surgeons, Columbia

University, New York, NY, 10032, USA

Nature (London, United Kingdom) (2002), 416(6881), SOURCE:

648-652

CODEN: NATUAS; ISSN: 0028-0836

PUBLISHER: Nature Publishing Group

DOCUMENT TYPE: Journal LANGUAGE: English

: 28 REFERENCE COUNT: THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s usp7

40 USP7 L3

=> s 13 and MDM2

2970 MDM2

8 L3 AND MDM2

=> d ibib 1-8 ·

ANSWER 1 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN

2006:197641 CAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER: 144:288171

TITLE: Molecular recognition of p53 and MDM2 by

USP7/HAUSP

AUTHOR(S): Sheng, Yi; Saridakis, Vivian; Sarkari, Feroz; Duan,

Shili; Wu, Tianne; Arrowsmith, Cheryl H.; Frappier,

Lori

Department of Medical Biophysics, Ontario Cancer CORPORATE SOURCE:

Institute, Toronto, ON, M5G 1L7, Can.

Nature Structural & Molecular Biology (2006), 13(3), SOURCE:

285-291

CODEN: NSMBCU; ISSN: 1545-9993

PUBLISHER: Nature Publishing Group

DOCUMENT TYPE: Journal LANGUAGE: English

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 2 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:156572 CAPLUS

DOCUMENT NUMBER: 145:119254

TITLE: Structural basis of competitive recognition of p53 and

MDM2 by HAUSP/USP7: implications for the regulation of the p53-MDM2 pathway

Hu, Min; Gu, Lichuan; Li, Muyang; Jeffrey, Philip D.; AUTHOR(S):

Gu, Wei; Shi, Yigong

CORPORATE SOURCE: Department of Molecular Biology, Lewis Thomas

Laboratory, Princeton University, Princeton, NJ, USA

PLos Biology (2006), 4(2), 228-239 CODEN: PBLIBG; ISSN: 1545-7885 SOURCE:

URL: http://biology.plosjournals.org/archive/1545-7885/4/2/pdf/10.1371 1545-7885 4 2 complete.pdf

PUBLISHER: Public Library of Science

Journal; (online computer file) DOCUMENT TYPE:

English LANGUAGE:

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1056192 CAPLUS

DOCUMENT NUMBER: 143:455700

TITLE: Reciprocal activities between herpes simplex virus

type 1 regulatory protein ICPO, a ubiquitin E3 ligase,

and ubiquitin-specific protease USP7

AUTHOR(S): Boutell, Chris; Canning, Mary; Orr, Anne; Everett,

Roger D.

CORPORATE SOURCE: MRC Virology Unit, Institute of Virology, Glasgow, G11

5JR, UK

SOURCE: Journal of Virology (2005), 79(19), 12342-12354

CODEN: JOVIAM; ISSN: 0022-538X American Society for Microbiology

DOCUMENT TYPE: Journal

PUBLISHER:

LANGUAGE: English

REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:327153 CAPLUS

DOCUMENT NUMBER: 143:2872

TITLE: Structure of the p53 binding domain of HAUSP/

USP7 bound to Epstein-Barr nuclear antigen 1: Implications for EBV-mediated immortalization

AUTHOR(S): Saridakis, Vivian; Sheng, Yi; Sarkari, Feroz;

Holowaty, Melissa N.; Shire, Kathy; Nguyen, Tin; Zhang, Rongguang G.; Liao, Jack; Lee, Weontae; Edwards, Aled M.; Arrowsmith, Cheryl H.; Frappier,

Lori

CORPORATE SOURCE: Department of Medical Genetics and Microbiology,

University of Toronto, Toronto, ON, M5S 1A8, Can.

SOURCE: Molecular Cell (2005), 18(1), 25-36

CODEN: MOCEFL; ISSN: 1097-2765

PUBLISHER: Cell Press
DOCUMENT TYPE: Journal
LANGUAGE: English

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:60430 CAPLUS

DOCUMENT NUMBER: 142:215611

TITLE: HAUSP is required for p53 destabilization

AUTHOR(S): Cummins, Jordan M.; Vogelstein, Bert

CORPORATE SOURCE: The Howard Hughes Medical Institute, The Sidney Kimmel

Comprehensive Cancer Center, Program in Cellular and Molecular Medicine, The Johns Hopkins University

Medical Institutions, Baltimore, MD, USA

Cell Cycle (2004), 3(6), 689-692

CODEN: CCEYAS; ISSN: 1538-4101

PUBLISHER: Landes Bioscience

DOCUMENT TYPE: Journal LANGUAGE: English

SOURCE:

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1997 CAPLUS

DOCUMENT NUMBER: 142:111841

TITLE: Gene expression profiles and biomarkers for the

detection of depression-related and other disease-related gene transcripts in blood

INVENTOR(S): Liew, Choong-Chin

PATENT ASSIGNEE(S): Chondrogene Limited, Can.

SOURCE: U.S. Pat. Appl. Publ., 154 pp., Cont.-in-part of U.S.

Ser. No. 802,875.

CODEN: USXXCO

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2004265868 US 2004014059 US 2006134635 US 2005191637 US 2005196762 US 2005196763 US 2005196764	A1 A1 A1 A1 A1 A1 A1	20041230 20040122 20060622 20050901 20050908 20050908	US 2004-812702 US 2002-268730 US 2004-802875 US 2004-803737 US 2004-803759 US 2004-803857 US 2004-803858	•	20040330 20021009 20040312 20040318 20040318 20040318 20040318
US 2005208505 PRIORITY APPLN. INFO.:	A1	20050922	US 2004-803648 US 1999-115125P US 2000-477148 US 2002-268730 US 2003-601518 US 2004-802875 US 2001-271955P US 2001-275017P US 2001-305340P US 2002-85783	A2	20040318 19990106 20000104 20021009 20030620 20040312 20010228 20010312 20010713 20020228

ANSWER 7 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN

2004:900604 CAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER:

142:4278

TITLE:

HAUSP/USP7 as an Epstein-Barr virus target

AUTHOR(S): Holowaty, M. N.; Frappier, L.

CORPORATE SOURCE:

Department of Medical Genetics and Microbiology,

University of Toronto, Toronto, Can.

SOURCE:

Biochemical Society Transactions (2004), 32(5),

731-732

CODEN: BCSTB5; ISSN: 0300-5127

PUBLISHER:

Portland Press Ltd.

DOCUMENT TYPE:

Journal

LANGUAGE:

English

REFERENCE COUNT:

15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 8 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

2000:114335 CAPLUS

DOCUMENT NUMBER:

132:332744

TITLE: AUTHOR(S): A genome-wide survey of RAS transformation targets Zuber, Johannes; Tchernitsa, Oleg I.; Hinzmann, Bernd; Schmitz, Anne-Chantal; Grips, Martin; Hellriegel,

Martin; Sers, Christine; Rosenthal, Andre; Schafer,

Reinhold

CORPORATE SOURCE:

Laboratory of Molecular Tumour Pathology, Institute of

Pathology, Charite, Humboldt-University, Berlin,

D-10117, Germany

SOURCE:

Nature Genetics (2000), 24(2), 144-152

CODEN: NGENEC; ISSN: 1061-4036

PUBLISHER:

Nature America

DOCUMENT TYPE:

Journal

LANGUAGE:

English

REFERENCE COUNT:

31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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FULL ESTIMATED COST

SINCE FILE TOTAL ENTRY SESSION 30.31 30.52

FILE 'PCTFULL' ENTERED AT 15:12:56 ON 20 SEP 2006 COPYRIGHT (C) 2006 Univentio

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MOST RECENT UPDATE WEEK: 200637 <200637/EW>
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>>> FOR CHANGES IN PCTFULL PLEASE SEE HELP CHANGE (last updated April 10, 2006) <<<

>>> NEW PRICES IN PCTFULL AS OF 01 JULY 2006. FOR DETAILS, PLEASE SEE HELP COST <<<

=> s USP7

L5 37 USP7

=> s HAUSP

L6 34 HAUSP

=> s 16 or 15

L7 59 L6 OR L5

=> s MDM2 and 17

829 MDM2

L8 18 MDM2 AND L7

=> s screen? or ident?

194428 SCREEN?

478664 IDENT?

L9 532010 SCREEN? OR IDENT?

=> s 19 and 18

L10 18 L9 AND L8

=> s 110 not py>2002

444636 PY>2002

L11 5 L10 NOT PY>2002

=> d ibib 1-5

L11 ANSWER 1 OF 5 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 2002070742 PCTFULL ED 20020926 EW 200237
TITLE (ENGLISH): METHOD FOR THE DEVELOPMENT OF GENE PANELS FOR
DIAGNOSTIC AND THERAPEUTIC PURPOSES BASED ON THE

EXPRESSION AND METHYLATOIN STATUS OF THE GENES
TITLE (FRENCH): PROCEDE DE MISE AU POINT DE GROUPES D'ECHANTILLONS DE

GENES A DES FINS DE DIAGNOSTIC ET DE THERAPIE QUI SONT BASES SUR L'EXPRESSION ET L'ETAT DE METHYLATION DES

GENES

INVENTOR(S): OLEK, Alexander, Schroederstrasse 13/2, 10115 Berlin,

DE;

BERLIN, Kurt, Marienkaeferweg 4, 14532 Stahndorf, DE PATENT ASSIGNEE(S): EPIGENOMICS AG, Kastanienalle 24, 10435 Berlin, DE [DE,

AGENT: SCHOHE, Stefan\$, Boehmert & Boehmert, Pettenkoferstr.

20-22, 80336 Muenchen\$, DE

LANGUAGE OF FILING: English LANGUAGE OF PUBL.: English DOCUMENT TYPE: Patent

PATENT INFORMATION:

NUMBER KIND DATE WO 2002070742 A1 20020912

DESIGNATED STATES

W:

AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG UZ VN YU ZA ZM ZW

RW (ARIPO): RW (EAPO): RW (EPO):

AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE

TR

BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG

RW (OAPI): BF BJ CF CG CI CM GA GN GQ GW ML APPLICATION INFO.: WO 2002-EP2255 A 20020301 PRIORITY INFO.: US 2001-60/272,549 20010301 20010301

GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW

ANSWER 2 OF 5 ACCESSION NUMBER: TITLE (ENGLISH):

PCTFULL COPYRIGHT 2006 Univentio on STN 2002070741 PCTFULL ED 20020926 EW 200237

METHODS, SYSTEMS AND COMPUTER PROGRAM PRODUCTS FOR DETERMINING THE BIOLOGICAL EFFECT AND/OR ACTIVITY OF DRUGS, CHEMICAL SUBSTANCES AND/OR PHARMACEUTICAL COMPOSITIONS BASED ON THEIR EFFECT ON THE METHYLATION

STATUS OF THE DNA

TITLE (FRENCH):

PROCEDES, SYSTEMES ET PRODUITS PROGRAMMES INFORMATIQUES PERMETTANT DE DETERMINER L'EFFET BIOLOGIQUE ET/OU L'ACTIVITE DE MEDICAMENTS, DE SUBSTANCES CHIMIQUES ET/OU DE COMPOSITIONS PHARMACEUTIQUES, SUR LA BASE DE LEUR EFFET SUR L'ETAT DE METHYLATION DE L'ADN

INVENTOR(S):

OLEK, Alexander, Schroederstrasse 13/2, 10115 Berlin,

PATENT ASSIGNEE(S):

BERLIN, Kurt, Marienkaeferweg 4, 14532 Stahnsdorf, DE EPIGENOMICS AG, Kastanienallee 24, 10435 Berlin, DE

[DE, DE]

AGENT:

SCHOHE, Stefan\$, Boehmert & Boehmert,

Pettenkoferstrasse 20-22, 80336 Muenchen\$, DE

LANGUAGE OF FILING: LANGUAGE OF PUBL.: DOCUMENT TYPE: PATENT INFORMATION: English English Patent

KIND DATE NUMBER ______ WO 2002070741 A2 20020912

DESIGNATED STATES

W: .

AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG UZ VN YU ZA ZM ZW

RW (ARIPO): RW (ARIPO): RW (EAPO): GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW

AM AZ BY KG KZ MD RU TJ TM

AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE RW (EPO):

TR

RW (OAPI): BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG APPLICATION INFO.: WO 2002-EP2254 A 20020301 PRIORITY INFO.: US 2001-60/272,484 20010301 US 2001-60/272,484 20010301 PRIORITY INFO.:

L11 PCTFULL COPYRIGHT 2006 Univentio on STN ANSWER 3 OF 5 2002057414 PCTFULL ED 20020801 EW 200230 ACCESSION NUMBER: TITLE (ENGLISH): LEUKOCYTE EXPRESSION PROFILING TITLE (FRENCH): EVALUATION DU NIVEAU D'EXPRESSION LEUCOCYTAIRE INVENTOR(S): WOHLGEMUTH, Jay, 664 Hamilton Avenue, Palo Alto, CA 94301, US [US, US]; FRY, Kirk, 2604 Ross Road, Palo Alto, CA 94303, US [US, MATCUK, George, 141C Escondido Village, Stanford, CA 94305, US [US, US]; ALTMAN, Peter, 717 Evelyn Avenue, Albany, CA 94706, US [US, US]; PRENTICE, James, 120 Dolores Street, San Francisco, CA 94103, US [US, US]; PHILLIPS, Julie, 1090 Mirador Terrace, Pacifica, CA . 94044, US [US, US]; LY, Ngoc, 2000 Crystal Springs Road 15-14, San Bruno, CA 94066, US [US, US]; WOODWARD, Robert, 1828 Rheem Court, Pleasanton, CA 94588, US [US, US]; QUERTERMOUS, Thomas, 44 El Rey Road, Portola Valley, CA 94028, US [US, US]; JOHNSON, Frances, 44 El Rey Road, Portola Valley, CA 94028, US [US, US] BIOCARDIA, INC., 384 Oyster Point Boulevard, #4, South PATENT ASSIGNEE(S): San Francisco, CA 94080, US [US, US], for all designates States except US; WOHLGEMUTH, Jay, 664 Hamilton Avenue, Palo Alto, CA 94301, US [US, US], for US only; FRY, Kirk, 2604 Ross Road, Palo Alto, CA 94303, US [US, US], for US only; MATCUK, George, 141C Escondido Village, Stanford, CA 94305, US [US, US], for US only; ALTMAN, Peter, 717 Evelyn Avenue, Albany, CA 94706, US [US, US], for US only; PRENTICE, James, 120 Dolores Street, San Francisco, CA 94103, US [US, US], for US only; PHILLIPS, Julie, 1090 Mirador Terrace, Pacifica, CA 94044, US [US, US], for US only; LY, Ngoc, 2000 Crystal Springs Road 15-14, San Bruno, CA 94066, US [US, US], for US only; WOODWARD, Robert, 1828 Rheem Court, Pleasanton, CA 94588, US [US, US], for US only; QUERTERMOUS, Thomas, 44 El Rey Road, Portola Valley, CA 94028, US [US, US], for US only; JOHNSON, Frances, 44 El Rey Road, Portola Valley, CA 94028, US [US, US], for US only WARD, Michael, R.\$, Morrison & Foerster LLP, 425 Market AGENT: Street, San Francisco, CA 94105-2482\$, US LANGUAGE OF FILING: English LANGUAGE OF PUBL.: English DOCUMENT TYPE: Patent PATENT INFORMATION: KIND DATE NUMBER -----WO 2002057414 A2 20020725 DESIGNATED STATES AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR W: CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW RW (ARIPO): GH GM KE LS MW MZ SD SL SZ TZ UG ZW

AM AZ BY KG KZ MD RU TJ TM

RW (EAPO):

RW (EPO): AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR RW (OAPI): BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG APPLICATION INFO.: WO 2001-US47856 A 20011022 PRIORITY INFO.: US 2000-60/241,994 20001020 US 2001-60/296,764 20010608 ANSWER 4 OF 5 L11PCTFULL COPYRIGHT 2006 Univentio on STN ACCESSION NUMBER: 2000079267 PCTFULL ED 20020515 TITLE (ENGLISH): TREATMENT OF CANCER TITLE (FRENCH): TRAITEMENT ANTICANCEREUX INVENTOR(S): NIZETIC, Dean; GROET, JuergenRP: GILL JENNINGS & EVERY SCHOOL OF PHARMACY, UNIVERSITY OF LONDON; PATENT ASSIGNEE(S): NIZETIC, Dean; GROET, Juergen LANGUAGE OF PUBL.: English DOCUMENT TYPE: Patent PATENT INFORMATION: NUMBER KIND DATE _____ WO 2000079267 A2 20001228 DESIGNATED STATES W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW GH GM KE LS MW MZ SD SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG WO 2000-GB2446 A 20000622 GB 2000-0008161.2 20000403 APPLICATION INFO.: PRIORITY INFO.: GB 1999-9914589.8 19990622 L11 ANSWER 5 OF 5 PCTFULL COPYRIGHT 2006 Univentio on STN ACCESSION NUMBER: 2000073479 PCTFULL ED 20020515 TITLE (ENGLISH): A COMBINED GROWTH FACTOR-DELETED AND THYMIDINE KINASE-DELETED VACCINIA VIRUS VECTOR TITLE (FRENCH): VECTEUR DU VIRUS DE LA VACCINE COMBINANT DELETION DU FACTEUR DE CROISSANCE ET DELETION DE THYMIDINE KINASE INVENTOR(S): MCCART, J., Andrea; BARTLETT, David, L.; MOSS, BernardRP: NATAUPSKY, Steven, J. PATENT ASSIGNEE(S): THE GOVERNMENT OF THE UNITED STATES OF AMERICA, as represented by THE SECRETARY, DEPARTMENT OF HEALTH AND HUMAN SERVICES; MCCART, J., Andrea; BARTLETT, David, L.; MOSS, Bernard LANGUAGE OF PUBL.: English DOCUMENT TYPE: Patent PATENT INFORMATION: NUMBER . KIND DATE -----WO 2000073479 A1 20001207 DESIGNATED STATES AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ W: DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT

TZ UA UG US UZ VN YU ZA ZW GH GM KE LS MW MZ SD SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM

GA GN GW ML MR NE SN TD TG

APPLICATION INFO.: PRIORITY INFO.:

WO 2000-US14679 A 20000526 US 1999-60/137,126 19990528

=> d kwic 4

L11 ANSWER 4 OF 5 PCTFULL COPYRIGHT 2006 Univentio on STN

DETD . . . as p53, could perhaps explain the

link to deletions of USPs in solid tumours. De-ubiquitination could play a $\,$

major role in the Mdm2 mediated control of p53 levels and its activation $\dot{}$

mechanism, since the ubiquitin-mediated proteasome degradation of p53 is an important effector arm of. . .

In recent years a number of other protein modifying polypeptide tags have been identified. Many of these are related to ubiquitin and-have high

levels of identity and similarity (determined using the BLAST algorithm, for

instance) to ubiquitin itself. There is a recognised super family of such

proteins which. . .

human SUMO-1 (PIC1 1

Sentrin, hSmt3C), SUMO-2 (hSmt3A) and SUMO-3 (hSMT3B) belong to the same family of UbL proteins with approximately 50% identity between

themselves, and some 15-30% identity and 40-60% similarity in amino acid

sequence to ubiquitin (Lapenta et al. 1997, Mannen et al. 1996, Kamitani et

al. 1998, Saitoh. . .

Several UbL hydrolase enzymes have been identified which convert

precursor UbL to active UbL. Some such enzymes interact with ubiquitin itself as well as with other UbL's. Proteases involved in cleavage of conjugates of UbL with target protein have been identified for instance

SENP1 and SUSP-1, which were recently cloned (Kim et al. 2000, Gong et al. 2000a), and found to specifically cleave. . .

Valero, et al. (1 999) published after the first priority date of the present application, have, in parallel identified this gene and pointed out the

gene product's sequence homologies to known USIP's in the conserred peptide domains previously identified e.g. by d'Andrea et al (1998). They

postulate a role in Alzheimer's disease. This protein has the HUGO approved name USP25.

fusion protein of

the ubiquitin-like protein of interest and a detectable protein, and using the $\ensuremath{\mathsf{I}}$

usual separation and immune based or autoradiographic identification techniques.

the specified domains,

some level of sequence homology with sequence ID $\boldsymbol{1}$, for instance at least

20%, preferably at least 50%, identity with that sequence, and a level of similarity of at least 50%, preferably at least 70% or more with that sequence (in. . .

the corresponding mouse product, described in Valero, et al 1999 may be used or sequences which have the above levels of identity and similarity with such a sequence.

outside the

specified domains, some level of sequence homology with sequence ID 1 for instance at least 20%, preferably at least 50%, identity with that

sequence, and a level of similarity of at least 50%, preferably at least 70% or

more with that sequence (in. . . as the corresponding mouse product, described in

Valero, et al 1999 may be used or sequences which have the above levels of

identity and similarity with such a sequence.

Experimental

We identify a portion of human chromosome 21 homozygously deleted in non-small cell non carcinoma (NSCLC) for further study. The region contained the DNA. . . et al. We found a shared region of overlap (SRO) for the hemizygous loss in other NSCLC. The current work is

to identify genes in the SRO which have a potential role in tumour suppression.

The exposure was for 14 hr to Molecular Dynamics (Sunnyvale, CA) Phosphorimager screens. The I.M.A.G.E. Consortium (Lennon et al., 1996) cDNA clone ID 82471 0 and the Unigene clone A0021343 have been used as labelled. . .

Identification and cloning of USP26
Twelve sequenced exon-trapped products, when analysed using
BLAST-N against public sequence databases, revealed clusters of
overlapping clDNA clones. Sequences. . .

with the binding of USP25 to its natural ubiquitinated substrates, since this residue is conserved between all UCH-s and USP-s so far identified.

of the sequences found to be interacting, from the GenBank database are given in the table,
Table 1. Summary of frequency and identities of specific interacting proteins from human brain with USP25-C178A, detected using Yeast-Two-Hybrid technique
Summary of Results by Number of specific Accession number decreasing. . .

SUMO-

1 (PIC1 , Sentrin, hSmt3C), SUMO-2 (hSmt3A) and SUMO-3 (hSMT3B) belong to the same family of UbL proteins with approximately 50% identity between themselves, and some 15-30% identity and 40-60% similarity in

amino acid sequence to ubiquitin (Lapenta et al. 1997, Mannen et al. 1996, Kamitani et al. 1998, Saitoh. . Figure Legends Figure 1. Identification of the Shared Region of Overlap (S.R.O.) for hemizygous deletions in 21ql 1-q21 in NSCLCA Cytogenetic map, Not I long range physical. . the single key aminoacids in the Cys and His domains. Two reports show the localisations of the highly homologous sequences for the HAUSP gene to 3p2l (Kashuba, et al 1997) and 16pl 3 (Robinson, et al 1998), respectively. A. 1992. Ubiquitin-specific proteases of Saccharomyces cerevisiae. J. Biol Chem 267:23364 Baker, R.T., Wang, X-W., Woollatt, E., White, J.A. and Sutherlands, G.R. Identification, functional characterisation, and chromosomal localisation of USP15, a novel Human USP related to Unp Oncoprotein, and a systematic nomenclature for hUSP's. Genomics. T., Saito, A... Suzuki, M., Shinomiya, H., Suzuki, T., Takahashi, E., Tanigami, A., Ichiyama, A., Chung, C.H., Nakamura, Y., Tanaka, K. Identification and chromosomal assignment of USP1, gene encoding a human ubiquitin-specific protease. Genomics, 54:155-158, 1998. human chromosome 5q33-q34, UBH1, encodes a novel deubiquitinating enzyme. Genomics 49:411 Haupt Y, Maya R, Kazaz A, Oren M (1 997) Mdm2 promotes the degradation of p53, Nature 387:296 Ichikawa, H., Hosoda, F., Arai, Y., Shimizu, K., Ohira, M., and Ohki, Sumeqi J, Klein G, Zabarovsky ER, Kisselev L. 1997. Notl linking/jumping clones of human chromosome 3: mapping of the TFRC, RA137 and HAUSP genes to regions rearranged in leukemia and deleted in solid tumours. FEBS Lett 419:181-185. Assignment of herpesvirus-associated ubiquitin-specific protease gene HAUSP to human chromosome band 16p 13.3 by in situ hybridisation, Cytogenet. Cell Genet. 83:100.

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E5
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L12 1 "HAUSP PROTEASE"/CN

=> DIS L12 1 SQIDE

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L12 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2006 ACS on STN

109136-49-4 REGISTRY

Proteinase, ubiquitin conjugate (9CI) (CA INDEX NAME) OTHER NAMES:

DEN1 protease CN

CN Deneddylase

CN Deubiquination enzyme UBP1

```
Deubiquitinase
CN
CN
     Deubiquitinating enzyme
CN
     Deubiquitinating enzyme DUB-2
CN
     HAUSP protease
CN
     ISG15-specific protease UBP43
CN
     Otubain 1
CN
     Polyubiquitin proteinase
     Protease USP21
CN
CN
     Proteinase, ubiquitin-fusion protein
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     Ubiquitin conjugate protease
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SR
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LC
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DT.CA
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       (Process); PRP (Properties); USES (Uses)
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RLD.P
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IMAGE: 6408678)./CN
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IMAGE: 5543601)/CN
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COST IN U.S. DOLLARS
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                                                                   TOTAL
                                                       ENTRY
                                                                 SESSION
FULL ESTIMATED COST
                                                        8.42
                                                                   54.46
FILE 'MEDLINE' ENTERED AT 15:19:32 ON 20 SEP 2006
 FILE LAST UPDATED: 19 Sep 2006 (20060919/UP). FILE COVERS 1950 TO DATE.
 On December 11, 2005, the 2006 MeSH terms were loaded.
 The MEDLINE reload for 2006 is now (26 Feb.) available. For details
 on the 2006 reload, enter HELP RLOAD at an arrow prompt (=>).
 See also:
    http://www.nlm.nih.gov/mesh/
    http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html
    http://www.nlm.nih.gov/pubs/techbull/nd05/nd05 med data changes.html
    http://www.nlm.nih.gov/pubs/techbull/nd05/nd05 2006 MeSH.html
 OLDMEDLINE is covered back to 1950.
 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2006 vocabulary.
 This file contains CAS Registry Numbers for easy and accurate
 substance identification.
=> s HAUSP or (USP () 7)
            39 HAUSP
          4983 USP
            37 USPS
          5006 USP
                 (USP OR USPS)
       1527014 7
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L13
            39 HAUSP OR (USP (W) 7)
=> s HAUSP or (USP7)
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            47 USP7
L14
            55 HAUSP OR (USP7)
=> s MDM2
          2699 MDM2
=> s 115 and 114
            18 L15 AND L14
=> s 116 not py>2002
       2271354 PY>2002
                 (PY>20029999)
L17
             1 L16 NOT PY>2002
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=> d ibib

L17 ANSWER 1 OF 1 MEDLINE on STN

ACCESSION NUMBER: 2002212418 MEDLINE DOCUMENT NUMBER: PubMed ID: 11923872

TITLE: Deubiquitination of p53 by HAUSP is an important

pathway for p53 stabilization.

AUTHOR: Li Muyang; Chen Delin; Shiloh Ariel; Luo Jianyuan; Nikolaev

Anatoly Y; Qin Jun; Gu Wei

CORPORATE SOURCE: Institute for Cancer Genetics, and Department of Pathology,

College of Physicians & Surgeons, Columbia University, 1150

St Nicholas Avenue, New York, New York 10032, USA. Nature, (2002 Apr 11) Vol. 416, No. 6881, pp. 648-53.

Electronic Publication: 2002-03-31.

Journal code: 0410462. ISSN: 0028-0836.

PUB. COUNTRY: England: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200205

ENTRY DATE: Entered STN: 12 Apr 2002

Last Updated on STN: 18 May 2002 Entered Medline: 17 May 2002

=> d abs

SOURCE:

L17 ANSWER 1 OF 1 MEDLINE on STN

The p53 tumour suppressor is a short-lived protein that is maintained at AB low levels in normal cells by Mdm2-mediated ubiquitination and subsequent proteolysis. Stabilization of p53 is crucial for its tumour suppressor function. However, the precise mechanism by which ubiquitinated p53 levels are regulated in vivo is not completely understood. By mass spectrometry of affinity-purified p53-associated factors, we have identified herpesyirus-associated ubiquitin-specific protease (HAUSP) as a novel p53-interacting protein. HAUSP strongly stabilizes p53 even in the presence of excess Mdm2, and also induces p53-dependent cell growth repression and apoptosis. Significantly, HAUSP has an intrinsic enzymatic activity that specifically deubiquitinates p53 both in vitro and in vivo. In contrast, expression of a catalytically inactive point mutant of HAUSP in cells increases the levels of p53 ubiquitination and destabilizes p53. These findings reveal an important mechanism by which p53 can be stabilized by direct deubiquitination and also imply that HAUSP might function as a tumour suppressor in vivo through the stabilization of p53.

=> d his

(FILE 'HOME' ENTERED AT 15:06:58 ON 20 SEP 2006)

FILE 'CAPLUS' ENTERED AT 15:07:09 ON 20 SEP 2006

L1 21 S HAUSP AND MDM2 L2 6 S L1 NOT PY>2004

L3 40 S USP7

L4 8 S L3 AND MDM2

FILE 'PCTFULL' ENTERED AT 15:12:56 ON 20 SEP 2006

L5 37 S USP7 L6 34 S HAUSP L7 59 S L6 OR L5 L8 18 S MDM2 AND L7

L9 532010 S SCREEN? OR IDENT?

L10 18 S L9 AND L8

L11 5 S L10 NOT PY>2002

FILE 'REGISTRY' ENTERED AT 15:17:14 ON 20 SEP 2006

E "HAUSP"/CN 25

L12 1 S E4

E "USP7"/CN 25 E "USP 7"/CN 25 E "USP-7"/CN 25

FILE 'MEDLINE' ENTERED AT 15:19:32 ON 20 SEP 2006

L13 39 S HAUSP OR (USP () 7)

L14 55 S HAUSP OR (USP7)

L15 2699 S MDM2

=> file pctfull

COST IN U.S. DOLLARS

SINCE FILE TOTAL ENTRY SESSION

FULL ESTIMATED COST 3.73 58.19

FILE 'PCTFULL' ENTERED AT 15:24:49 ON 20 SEP 2006 COPYRIGHT (C) 2006 Univentio

FILE LAST UPDATED: 18 SEP 2006 <20060918/UP>
MOST RECENT UPDATE WEEK: 200637 <200637/EW>

FILE COVERS 1978 TO DATE

>>> IMAGES ARE AVAILABLE ONLINE AND FOR EMAIL-PRINTS <<<

>>> NEW IPC8 DATA AND FUNCTIONALITY NOW AVAILABLE IN THIS FILE.
SEE
http://www.stn-international.de/stndatabases/details/ipc-reform.html >>>

>>> FOR CHANGES IN PCTFULL PLEASE SEE HELP CHANGE (last updated April 10, 2006) <<<

>>> NEW PRICES IN PCTFULL AS OF 01 JULY 2006. FOR DETAILS, PLEASE SEE HELP COST <<<

=> d 111 ibib

L11 ANSWER 1 OF 5
ACCESSION NUMBER: 2002070742 PCTFULL ED 20020926 EW 200237
TITLE (ENGLISH): METHOD FOR THE DEVELOPMENT OF GENE PANELS FOR DIAGNOSTIC AND THERAPEUTIC PURPOSES BASED ON THE

EXPRESSION AND METHYLATOIN STATUS OF THE GENES

TITLE (FRENCH): PROCEDE DE MISE AU POINT DE GROUPES D'ECHANTILLONS DE

GENES A DES FINS DE DIAGNOSTIC ET DE THERAPIE QUI SONT BASES SUR L'EXPRESSION ET L'ETAT DE METHYLATION DES

GENES

INVENTOR(S): OLEK, Alexander, Schroederstrasse 13/2, 10115 Berlin,

DE;

BERLIN, Kurt, Marienkaeferweg 4, 14532 Stahndorf, DE

PATENT ASSIGNEE(S): EPIGENOMICS AG, Kastanienalle 24, 10435 Berlin, DE [DE,

DE]

AGENT: SCHOHE, Stefan\$, Boehmert & Boehmert, Pettenkoferstr.

20-22, 80336 Muenchen\$, DE

LANGUAGE OF FILING: English
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent

PATENT INFORMATION:

 DESIGNATED STATES

W:

AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG UZ VN YU ZA ZM ZW

GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW RW (ARIPO):

RW (EAPO): AM AZ BY KG KZ MD RU TJ TM

RW (EPO): AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE

TR

BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG

RW (OAPI): BF BJ CF CG C1 CF1 GA C... C2

APPLICATION INFO.: WO 2002-EP2255 A 20020301
US 2001-60/272,549 20010301

=> d l11 ibib 1-5

ANSWER 1 OF 5 ACCESSION NUMBER: TITLE (ENGLISH):

PCTFULL COPYRIGHT 2006 Univentio on STN 2002070742 PCTFULL ED 20020926 EW 200237 METHOD FOR THE DEVELOPMENT OF GENE PANELS FOR DIAGNOSTIC AND THERAPEUTIC PURPOSES BASED ON THE EXPRESSION AND METHYLATOIN STATUS OF THE GENES

TITLE (FRENCH):

PROCEDE DE MISE AU POINT DE GROUPES D'ECHANTILLONS DE GENES A DES FINS DE DIAGNOSTIC ET DE THERAPIE QUI SONT BASES SUR L'EXPRESSION ET L'ETAT DE METHYLATION DES

GENES

INVENTOR(S): OLEK, Alexander, Schroederstrasse 13/2, 10115 Berlin,

BERLIN, Kurt, Marienkaeferweg 4, 14532 Stahndorf, DE PATENT ASSIGNEE(S):

EPIGENOMICS AG, Kastanienalle 24, 10435 Berlin, DE [DE,

DE]

AGENT: SCHOHE, Stefan\$, Boehmert & Boehmert, Pettenkoferstr.

20-22, 80336 Muenchen\$, DE

LANGUAGE OF FILING: English English LANGUAGE OF PUBL.: DOCUMENT TYPE: Patent

PATENT INFORMATION:

· KIND DATE NUMBER -----WO 2002070742 . A1 20020912

DESIGNATED STATES

W:

AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG UZ VN YU ZA ZM ZW

GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW RW (ARIPO):

AM AZ BY KG KZ MD RU TJ TM RW (EAPO):

RW (EPO): AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE

TR

RW (OAPI): BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG

APPLICATION INFO.: WO 2002-EP2255 A 20020301 PRIORITY INFO.: US 2001-60/272,549 20010301

L11ANSWER 2 OF 5 ACCESSION NUMBER: TITLE (ENGLISH):

PCTFULL COPYRIGHT 2006 Univentio on STN 2002070741 PCTFULL ED 20020926 EW 200237

METHODS, SYSTEMS AND COMPUTER PROGRAM PRODUCTS FOR DETERMINING THE BIOLOGICAL EFFECT AND/OR ACTIVITY OF DRUGS, CHEMICAL SUBSTANCES AND/OR PHARMACEUTICAL COMPOSITIONS BASED ON THEIR EFFECT ON THE METHYLATION

STATUS OF THE DNA

TITLE (FRENCH): PROCEDES, SYSTEMES ET PRODUITS PROGRAMMES INFORMATIQUES

> PERMETTANT DE DETERMINER L'EFFET BIOLOGIQUE ET/OU L'ACTIVITE DE MEDICAMENTS, DE SUBSTANCES CHIMIQUES

ET/OU DE COMPOSITIONS PHARMACEUTIQUES, SUR LA BASE DE LEUR EFFET SUR L'ETAT DE METHYLATION DE L'ADN OLEK, Alexander, Schroederstrasse 13/2, 10115 Berlin, INVENTOR(S): BERLIN, Kurt, Marienkaeferweg 4, 14532 Stahnsdorf, DE EPIGENOMICS AG, Kastanienallee 24, 10435 Berlin, DE PATENT ASSIGNEE(S): [DE, DE] AGENT: SCHOHE, Stefan\$, Boehmert & Boehmert, Pettenkoferstrasse 20-22, 80336 Muenchen\$, DE LANGUAGE OF FILING: English LANGUAGE OF PUBL.: English DOCUMENT TYPE: Patent PATENT INFORMATION: KIND DATE NUMBER ------WO 2002070741 A2 20020912 DESIGNATED STATES W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG UZ VN YU ZA ZM ZW RW (ARIPO): GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW RW (EAPO): AM AZ BY KG KZ MD RU TJ TM RW (EPO): AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG RW (OAPI): APPLICATION INFO.: WO 2002-EP2254 A 20020301 PRIORITY INFO.: US 2001-60/272,484 20010301 COPYRIGHT 2006 Univentio on STN L11ANSWER 3 OF 5 PCTFULL 2002057414 PCTFULL ED 20020801 EW 200230 ACCESSION NUMBER: TITLE (ENGLISH): LEUKOCYTE EXPRESSION PROFILING TITLE (FRENCH): EVALUATION DU NIVEAU D'EXPRESSION LEUCOCYTAIRE INVENTOR(S): WOHLGEMUTH, Jay, 664 Hamilton Avenue, Palo Alto, CA 94301, US [US, US]; FRY, Kirk, 2604 Ross Road, Palo Alto, CA 94303, US [US, MATCUK, George, 141C Escondido Village, Stanford, CA 94305, US [US, US]; ALTMAN, Peter, 717 Evelyn Avenue, Albany, CA 94706, US [US, US]; PRENTICE, James, 120 Dolores Street, San Francisco, CA 94103, US [US, US]; PHILLIPS, Julie, 1090 Mirador Terrace, Pacifica, CA 94044, US [US, US]; LY, Ngoc, 2000 Crystal Springs Road 15-14, San Bruno, CA 94066, US [US, US]; WOODWARD, Robert, 1828 Rheem Court, Pleasanton, CA 94588, US [US, US]; QUERTERMOUS, Thomas, 44 El Rey Road, Portola Valley, CA 94028, US [US, US]; JOHNSON, Frances, 44 El Rey Road, Portola Valley, CA 94028, US [US, US] PATENT ASSIGNEE(S): BIOCARDIA, INC., 384 Oyster Point Boulevard, #4, South San Francisco, CA 94080, US [US, US], for all designates States except US; WOHLGEMUTH, Jay, 664 Hamilton Avenue, Palo Alto, CA 94301, US [US, US], for US only; FRY, Kirk, 2604 Ross Road, Palo Alto, CA 94303, US [US, US], for US only; MATCUK, George, 141C Escondido Village, Stanford, CA 94305, US [US, US], for US only;

ALTMAN, Peter, 717 Evelyn Avenue, Albany, CA 94706, US

```
[US, US], for US only;
                         PRENTICE, James, 120 Dolores Street, San Francisco, CA
                         94103, US [US, US], for US only;
                         PHILLIPS, Julie, 1090 Mirador Terrace, Pacifica, CA
                         94044, US [US, US], for US only;
                         LY, Ngoc, 2000 Crystal Springs Road 15-14, San Bruno,
                         CA 94066, US [US, US], for US only;
WOODWARD, Robert, 1828 Rheem Court, Pleasanton, CA
                         94588, US [US, US], for US only;
                         QUERTERMOUS, Thomas, 44 El Rey Road, Portola Valley, CA
                         94028, US [US, US], for US only;
                         JOHNSON, Frances, 44 El Rey Road, Portola Valley, CA
                         94028, US [US, US], for US only
                         WARD, Michael, R.$, Morrison & Foerster LLP, 425 Market
AGENT:
                         Street, San Francisco, CA 94105-2482$, US
LANGUAGE OF FILING:
                         English
                         English
LANGUAGE OF PUBL.:
DOCUMENT TYPE:
                         Patent
PATENT INFORMATION:
                         NUMBER KIND DATE
                         WO 2002057414 A2 20020725
DESIGNATED STATES
                         AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR
       W:
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                         SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
       RW (ARIPO):
RW (EAPO):
RW (EPO):
                        GH GM KE LS MW MZ SD SL SZ TZ UG ZW
                        AM AZ BY KG KZ MD RU TJ TM
                        AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
                         TR
RW (OAPI): BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG
APPLICATION INFO.: WO 2001-US47856 A 20011022
PRIORITY INFO.: US 2000-60/241,994 20001020
US 2001-60/296.764 20010608
                         US 2001-60/296,764
                                                  20010608
       ANSWER 4 OF 5 . PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 20000/920/ FOLLAR TREATMENT OF CANCER ANTICANCE
L11
                        2000079267 PCTFULL ED 20020515
TITLE (FRENCH):
                       TRAITEMENT ANTICANCEREUX
INVENTOR(S):
                       NIZETIC, Dean;
                     • GROET, JuergenRP : GILL JENNINGS & EVERY
PATENT ASSIGNEE(S):
                       SCHOOL OF PHARMACY, UNIVERSITY OF LONDON;
                         NIZETIC, Dean;
                         GROET, Juergen
LANGUAGE OF PUBL.:
                         English
DOCUMENT TYPE:
                         Patent
PATENT INFORMATION:
                                 KIND DATE
                         NUMBER
                         -----
                         WO 2000079267
                                             A2 20001228
DESIGNATED STATES
       W:
                         AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU
                         CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN
                         IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK
                         MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM
                         TR TT TZ UA UG US UZ VN YU ZA ZW GH GM KE LS MW MZ SD
                         SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY
                         DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG
                         CI CM GA GN GW ML MR NE SN TD TG
APPLICATION INFO.:
                         WO 2000-GB2446 A 20000622
PRIORITY INFO.:
                         GB 2000-0008161.2 20000403
GB 1999-9914589.8 19990622
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L11 ANSWER 5 OF 5 PCTFULL COPYRIGHT 2006 Univentio on STN ACCESSION NUMBER: 2000073479 PCTFULL ED 20020515 TITLE (ENGLISH): A COMBINED GROWTH FACTOR-DELETED AND THYMIDINE KINASE-DELETED VACCINIA VIRUS VECTOR VECTEUR DU VIRUS DE LA VACCINE COMBINANT DELETION DU TITLE (FRENCH): FACTEUR DE CROISSANCE ET DELETION DE THYMIDINE KINASE INVENTOR(S): MCCART, J., Andrea; BARTLETT, David, L.; MOSS, BernardRP: NATAUPSKY, Steven, J. PATENT ASSIGNEE(S): THE GOVERNMENT OF THE UNITED STATES OF AMERICA, as represented by THE SECRETARY, DEPARTMENT OF HEALTH AND HUMAN SERVICES; MCCART, J., Andrea; BARTLETT, David, L.; MOSS, Bernard LANGUAGE OF PUBL.: English DOCUMENT TYPE: Patent PATENT INFORMATION: NUMBER KIND DATE _______ WO 2000073479 A1 20001207 DESIGNATED STATES AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW GH GM KE LS MW MZ SD SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG WO 2000-US14679 A 20000526 US 1999-60/137,126 19990528 APPLICATION INFO.: PRIORITY INFO.: => d lll ibib kwic 2 L11 ANSWER 2 OF 5
ACCESSION NUMBER: L11 ANSWER 2 OF 5 PCTFULL COPYRIGHT 2006 Univentio on STN 2002070741 PCTFULL ED 20020926 EW 200237 TITLE (ENGLISH): METHODS, SYSTEMS AND COMPUTER PROGRAM PRODUCTS FOR DETERMINING THE BIOLOGICAL EFFECT AND/OR ACTIVITY OF DRUGS, CHEMICAL SUBSTANCES AND/OR PHARMACEUTICAL COMPOSITIONS BASED ON THEIR EFFECT ON THE METHYLATION STATUS OF THE DNA TITLE (FRENCH): PROCEDES, SYSTEMES ET PRODUITS PROGRAMMES INFORMATIOUES PERMETTANT DE DETERMINER L'EFFET BIOLOGIQUE ET/OU L'ACTIVITE DE MEDICAMENTS, DE SUBSTANCES CHIMIQUES ET/OU DE COMPOSITIONS PHARMACEUTIQUES, SUR LA BASE DE LEUR EFFET SUR L'ETAT DE METHYLATION DE L'ADN INVENTOR(S): OLEK, Alexander, Schroederstrasse 13/2, 10115 Berlin, BERLIN, Kurt, Marienkaeferweg 4, 14532 Stahnsdorf, DE PATENT ASSIGNEE(S): EPIGENOMICS AG, Kastanienallee 24, 10435 Berlin, DE [DE, DE] AGENT: SCHOHE, Stefan\$, Boehmert & Boehmert, Pettenkoferstrasse 20-22, 80336 Muenchen\$, DE LANGUAGE OF FILING: English

PATENT INFORMATION:

LANGUAGE OF PUBL.:

DOCUMENT TYPE:

NUMBER KIND DATE

WO 2002070741 A2 20020912

English

Patent

DESIGNATED STATES

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG UZ VN YU ZA ZM ZW RW (ARIPO): GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW RW (EAPO): AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE RW (EPO): TRRW (OAPI): BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG APPLICATION INFO.: WO 2002-EP2254 A 20020301 PRIORITY INFO.: US 2001-60/272,484 20010301 . . since in most of the cases an effective drug/treatment has to be found very rapidly, Furthermore, such developments currently involve very cost-intensive screening procedures until a particularly suited compound (often called Jead"-cornpound) is.found which could then serve as a chemical basis for an effective treatment. of course, alternative treatments for already known diseases. Furthermore, the need exists for a reliable, costeffective, fast and autornateable method for screening such new effective compounds. 2. Screening for new biologically active compounds using , combinatorial chemistry" The method of combinatorial chemistry is described as a profound change in the. . . AT, et al. , Search and discovery strategies for biotechnology: the paradigm shift. " Microbiol Mol Biol Rev 2000 Sep; 64(3):573-606) In general, combinatorial chemistry involves screening of a specific (or a set of specific) compound with a vast number of otential biological candidate substances for example, proteins) that might interact with the compound. Interacting partners are selected and used for further screening. Initially screened and isolated compounds can be used as Jead" compounds for the development of biologically active compounds useful for treatment of diseases. potential utility for the treatment of conditions involving cerebral hypoxia. Equot; Life Sci 2000 Aug 1 1;67(12):1389-96) describe the use of HTS (high-throughput screening) libraries for reevaluation of the pharmacologic properties of substances such as extract from the leaves of Ginkgo biloba Linne (form.. Although the method of combinatorial chemistry exhibits several advantages in comparison to conventional methods for screening for biologically effective compounds which are useful for the development of new medicaments, there are still several drawbacks associated with this method.

The screening of a combinatorial chemistry library involves a

screening for a multitude of different possible reactions and/or interactions of the comp6unds to be analysed with the in-teracting partners. Therefore, the reaction conditions are assumed

teracting partners. Therefore, the reaction conditions are assumed crucial for the result of the

screening. In particular, a compound which shows an interaction with a target in such a corn-binatorial assay in vitro might exhibit. . . prediction of an effective compound very difficult and unreliable. As a result, an interaction in an in vitro combinatorial chemistry screening assay can always only give a hint for a potential biological function of the screened compound in vivo.

As a result, combinatorial chemistry screening involves a necessary second step; once a potential target/lead compound has been identified/found, the biological effect still has to be confirmed/determined in an in vivo context. This makes compound identification using this method unpredictable, slow and costly.

only individual regions
up to approximately 3000 base pairs in length have been examined, and an overall examination of cells to identify thousands of possible methylation events is not-possible. However,

this method is not capable of reliably analyzing minute fragments from small. . .

Burkitt's lym-

phorna: molecular analysis of primary tumor tissue" Blood 1998 Feb 15;91(4):13 73-8 1)

- Wilms tumor (Kleymenova EV et al. " Identification of a tumor-specific methylation site in

the Wilms tumor suppressor gene" Oncogene 1998 Feb 12;16(6):713-20) - Prader-Willi/Angelman syndrome (Zeschnigh et al. "Imprinted. .

The. present invention uses the modifications in the methylation pattern of the DNA for

screening of biologically effective substances. In general, the invention uses the fact that the biological effect of a potentially biologically effective drug,. .

The invention has several advantages in comparison to other. screening methods, in particular combinatorial chemistry. First, the reaction conditions of the drug, chemical substance or pharmaceutical composition with the biological test system. . .

Second, the analysis of the methylation pattern of the DNA allows screening of the in vivo effect of the substance in a one-step procedure using one controllable reaction (namely, the bisulfite treatment in order. . .

Thirdly, screening for potential lead-compounds becomes less time consuming and less costly, since the complete screening and analysis procedure can be automated.

Fourth, the inventive method allows the inclusion of personal data into the selection/analysis

procedure which allows for a personalised screening of drugs, chemical substances or pharmaceutical compositions.

In a further preferred method according to the invention, the biological samples A and B are obtained from the identical individual, tissue, cell or other biological material.

or

pharmaceutical composition. This allows the use of the inventive method to monitor and/or modify an already employed treatment regimen and to screen for unwanted side effects of the initially employed drugs, chemical substances or p harmaceutical compositions which leads to a strictly ,personalised" medicament. . .

cytosine methylation sites is analysed in parallel. The analysis of a multitude of sites in parallel allows for both an effective screening and a statistically highly relevant result of the method.

one to directly connect the tested drug, chemical substance or pharmaceutical composition with an effect on those genes and therefore allow the identification of possibly valuable new lead compounds as well as therapeutically important compounds.

In one embodiment, the method of the invention is characterised in that the identical biologi-cal sample, different biological samples or a combination thereof is used in steps a) and/or b).

Example 2

Screening of a peptide library
A peptide library was prepared in a 96-well culture plate which
contained overlapping peptide
fragments derived from the. . .

micro arrays representing 256 CpG and the inethylation statuses of the CpGs were analysed according to a method described in Example 3 $\,$

Screening of a fractionated plant crude extract In order to analyse the anti-metastatic effect of Celosia argentea seed extracts (CAE), which have traditionally. . .

(CD47 anti-

gen (Rh-related antigen, integrin-associated signal transducer); CD48 (CD48 antigen (B-cell membrane protein); CD53 (CD53 antigen); CD59 (CD59 antigen p18-20 (antigen identified by monoclonal antibodies 16.3A5, EJ16, EBO, EL32 and G344); CD63 (CD63 antigen (me-lanoma I antigen); CD68 (CD68 antigen); CD7 (CD7 antigen. . . LAMA4 (Laminin, alpha 4); LAMA5 (Laminin, alpha 5); LY64 (Lymphocyte antigen 64 (mouse) homolog, radioprotective, 105kD); LYZ (Lysozyme (renal amyloidosis)); MDUI (Antigen identified by monoclonal antibodies 4F2, TRAI.10, TROP4, and T43); MET (Met proto-oncogene (hepatocyte growth factor

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receptor)); MIC2
(Antigen identified by monoclonal antibodies 12E7, F21 and
013); MICA (MHC class I po-
lypeptide-related sequence A); MME (Membrane metallo-endopeptidase
(neutral endopepti-
dase, enkephalinase,.
I (BCL2-
related)); MCM4 (Minichromosome maintenance deficient (S. cerevisiae)
4); MEKK3
(MAP/ERK kinase kinase 3); MEKK5 (MAP/ERK kinase kinase 5); MKI67
(Antigen identi-
fied by monoclonal antibody Ki-67); MSTIR (Mdcrophage stimulating 1
receptor (c-met-
related tyrosine kinase)); NCKI (NCK adaptor protein 1); NEK3 (NIMA
(never. .
of split);
AFD I (Acrofacial dysostosis 1, Nager type); AGC I (Aggrecan I
(chondroitin sulfate proteo-
glycan 1, large aggregating proteoglycan, antigen identified
by monoclonal antibody AO 1 22));
AH02 (Albright hereditary osteodystrophy-2); A1113 (Amelogenesis
imperfecta 3, hypoinatu-
ration or hypoplastic type); ALX3 (Aristaless-like horneobox. . .
related
to AF4); LYLI (Lymphoblastic, leukemia derived sequence 1); MAFG (V-maf
musculoapo-
neurotic fibrosarcoma (avian) oncogene family, protein G); MAX (MAX
protein); MDM2
(Mouse double minute 2, human homolog of; p53-binding protein); MHC2TA
(MHC class II
transactivator); MKI67 (Antigen identified by monoclonal
antibody Ki-67); MNDA (Myeloid
cell nuclear differentiation antigen); MSXI (Msh (Drosophila) homeo box
homolog I (for-
merly homeo box 7));. . .
integrin-associated
signal transducer)); CD5 (CD5 antigen (p56-62)); CD53 (CD53 antigen);
CD58 (CD58 anti-
gen, (lymphocyte function-associated antigen 3)); CD59 (CD59 antigen
p18-20 (antigen
  identified by monoclonal antibodies 16.3A5, EJ16, EJ30, EL32
and G344)); CD5L (CD5 an-
tigen-like (scavenger receptor cysteine rich family)); CD6 (CD6
antigen);.
LYN (V-yes-1
Yamaguchi sarcoma viral related oncogene hornolog); LYZ (Lysozyme (renal
amyloidosis))-,
MISI (Membrane component, chromosome 1, surface marker I (400
glycoprotein, identi-
fied by monoclonal antibody GA733)); MAB21L1 (Mab-21 (C. elegans)-like
1); MACAMI
(Mucosal addressin cell adhesion molecule-1); MADHI (MAD (mothers
against decapentap-
legic, Drosophila).
                    . . MCC (Mutated in colorectal cancers); MCF2
(MCF.2 cell line derived
transforming sequence); MCP (Membrane cofactor protein (CD46,
trophoblast-lymphocyte
cross-reactive antigen)); MDF1 (Antigen identified by
monoclonal antibody A-3A4); MDH2
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(Malate dehydrogenase 2, NAD (mitochondrial)); MDUI (Antigen

    identified by monoclonal

  antibodies 4172, TRALIO, TROP4, and T43); MEI (Malic enzyme 1, soluble);
  ME2 (Malic
  enzyme 2, mitochondrial); MEKKI (MAP/ERK kinase kinase. . . MEMOI
  (Methylation modifier for class I HLA); MENI (Multiple endocrine
  neoplasia 1); MEPIA (Meprin A, alpha (PABA peptide hydrolase)); MER2
  (Antigen identi-
  fied by monoclonal antibodies 1D12, 2177); MFAP2 (Microfibrillar-
  associated protein 2);
  MFAP4 (Microfibrillar-associated protein 4); MFTS (Migraine, familial
  typical, susceptibility
  to); MGCT ( MGI); MGP (Matrix Gla protein); MHC2TA (MHC class 11
  transactivator);
  MIC2 (Antigen identified by monoclonal antibodies 12E7, F21
  and 013); MI C5 (Antigen
    identified by monoclonal antibody RI); MIC7 (Antigen
  identified by monoclonal antibody
  28 7); MICA (MHC class I polypeptide-related sequence A); MIF
  (Macrophage migration
  inhibitory factor (glycosylation-inhibiting factor)); MIG (Monokine
  induced.
  (Uridine phosphorylase); UPKlB (Uropla-
  kin 113); UROD (Uroporphyrinogen decarboxylase); UROS (Uroporphyrinogen
  III synthase
  (congenital erythropoietic porphyria)); USH2A (Usher syndrome 2A
  (autosornal recessive,
  mild)); USP7 (Ubiquitin specific protease 7 (herpes
  virus-associated)); VASP (Vasodilator-
  stimulated phosphoprotein); VCAM I (Vascular cell adhesion molecule 1);
  VDAC I (Voltage-
  dependent anion.
  CD48 (CD48 an-
  tigen (B-cell membrane protein)); CD53 (CD53 antigen); CD58 (CD58
  antigen, (lymphocyte
  function-associated antigen 3)); CD59 (CD59 antigen p18-20 (antigen
  identified by monoclo-
  nal antibodies 16.3A5, EJ16, EJ30, EL32 and G344)); CD63 (CD63 antigen
  (melanoma 1
  antigen)); CD68 (CD68 antigen); CD7 (CD7 antigen. . . gene 3); LY64
  (Lymphocyte antigen 64 (mouse) ho-
  molog, radioprotective, 105kD); LYZ (Lysozyme (renal amyloidosis));
  MAPIB (Microtubu-
  le-associated protein 113); MDUI (Antigen identified by
  monoclonal antibodies 4172,
  TRALIO, TROP4, and T43); MIC2 (Antigen identified by
  monoclonal antibodies 12E7, F21
  and 013); MICA (MHC class I polypeptide-related sequence A); MME
  (Membrane metallo-
  endopeptidase (neutral endopeptidase, enkephalinase, CALLA,.
  melanogaster muscleblind B protein); MDM2 (Mouse double minute
  2, human homolog of,
  p53-binding protein); MHC2TA (MHC class 11 transactivator); MKI67
  (Antigen identified by
  monoclonal antibody Ki-67); MNDA (Myeloid cell nuclear differentiation
  antigen); MSX1
  (Msh (Drosophila) homeo box homolog 1 (formerly homeo box 7)); MTHFD.
  member 3)); LYN (V-yes-1 Yamaguchi sarcoma viral related oncogene
  homolog); MIS I (Membrane component, chromosome 1, surface marker I
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tein, identified by monoclonal antibody GA733)); M4SI
       (Membrane component, chromoso-
       mal 4, surface marker (35kD glycoprotein)); MADH4 (MAD (mothers against
       decapentaple-
       gic, Drosophila) homolog. . . oncogene: family, protein
       K); MASI (MASI oncogene); MAX (MAX protein); MCC (Mutated in colorectal
       cancers);
       MCF2 (MCF.2 cell line derived transforming sequence); MDM2
       (Mouse double minute 2,
       human homolog of-, p53-binding protein); MEL (Mel transforming oncogene
       (derived from
       cell line NK14) - RAB8 homolog); MELLI (Mel. . . mem-
       ber 1)); LTB (Lymphotoxin beta (TNF superfamily, member 3)); MIS I
       (Membrane compo-
       nent, chromosome 1, surface marker I (40kD glycoprotein,
       identified by monoclonal antibody
       GA733)); M4SI (Membrane component, chromosomal 4, surface marker (35kD
       glycopro-
       tein)); MADH4. (MAD (mothers against decapentaplegic, Drosophila)
       homolog 4);. . .
CLMEN.
       . . according to any of claims I to 4, characierised in that the
       biological samples A
       and B are obtained from the identical individual, tissue, cell
       or other biological material.
       . Method according claim 5, characterised in that the biological samples
       A. and B. .
       28 Method according to any of claims I to 27, characterised in that the
       identical biological
       sample, different biological samples or a combination thereof is used in
       steps a) and/or b).
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L2
             6 S L1 NOT PY>2004
L3
             40 S USP7
L4
              8 S L3 AND MDM2
    FILE 'PCTFULL' ENTERED AT 15:12:56 ON 20 SEP 2006
L5
             37 S USP7
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             34 S HAUSP
L7
             59 S L6 OR L5
rs
             18 S MDM2 AND L7
L9
         532010 S SCREEN? OR IDENT?
L10
             18 S L9 AND L8
L11
              5 S L10 NOT PY>2002
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               E "USP7"/CN 25
                E "USP 7"/CN 25
                E "USP-7"/CN 25 ·
     FILE 'MEDLINE' ENTERED AT 15:19:32 ON 20 SEP 2006
L13
             39 S HAUSP OR (USP () 7)
L14
             55 S HAUSP OR (USP7)
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(40kD glycopro-

L15 2699 S MDM2

L16 18 S L15 AND L14 L17 1 S L16 NOT PY>2002

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ACCESSION NUMBER: 2002:312567 CAPLUS

DOCUMENT NUMBER: 137:44608

TITLE: Deubiquitination of p53 by HAUSP is an important pathway for p53 stabilization

AUTHOR(S): Li, Muyang; Chen, Delin; Shiloh, Ariel; Luo, Jianyuan;

Nikolaev, Anatoly Y.; Qin, Jun; Gu, Wei

CORPORATE SOURCE: Institute for Cancer Genetics, and Department of

Pathology, College of Physicians b Surgeons, Columbia

University, New York, NY, 10032, USA

SOURCE: Nature (London, United Kingdom) (2002), 416(6881),

648-652

CODEN: NATUAS; ISSN: 0028-0836

PUBLISHER: Nature Publishing Group

DOCUMENT TYPE: Journal LANGUAGE: English

The p53 tumor suppressor is a short-lived protein that is maintained at low levels in normal cells by Mdm-mediated ubiquitination and subsequent proteolysis. Stabilization of p53 is crucial for its tumor suppressor function. However, the precise mechanism by which ubiquitinated p53 levels are regulated in vivo is not completely understood. By mass spectrometry of affinity-purified p53-associated factors, the authors have identified herpesvirus-associated ubiquitin-specific protease (HAUSP) as a novel p53-interacting protein. HAUSP strongly stabilizes p53 even in the presence of excess Mdm2, and also induces p53-dependent cell growth repression and apoptosis. Significantly, HAUSP has an intrinsic enzymic activity that specifically

deubiquitinates p53 both in vitro and in vivo. In contrast, expression of a catalytically inactive point mutant of HAUSP in cells increases the levels of p53 ubiquitination and destabilizes p53. These findings reveal an important mechanism by which p53 can be stabilized by direct deubiquitination and also imply that HAUSP might function as a tumor suppressor in vivo through the stabilization of p53.

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